Intermediate Application No
PCT/EP2004/011269

A. CLASSIFICATION OF SUBJECT MATTER I PC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

#### **B. FIELDS SEARCHED**

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	WO 02/060942 A (INCYTE GENOMICS, INC; WARREN, BRIDGET, A; HONCHELL, CYNTHIA, D;	1-12 ~
A	LU, YA) 8 August 2002 (2002-08-08)	19,20
X	abstract; claims 1-87 page 10, line 16 - page 15, line 12 & DATABASE GENESEQ 5 November 2002 (2002-11-05),	1-12
A	retrieved from EMBL Database accession no. ABG76508 abstract	19,20
х	WO 03/029405 A (HYSEQ, INC; TANG, Y., TOM;	1-12
A	NUVELO) 10 April 2003 (2003-04-10)  abstract page 3, line 31 - page 8, line 14 claims 1-7	19,20

X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
<ul> <li>Special categories of cited documents:</li> <li>"A" document defining the general state of the art which is not considered to be of particular relevance</li> <li>"E" earlier document but published on or after the international filing date</li> <li>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</li> <li>"O" document referring to an oral disclosure, use, exhibition or other means</li> <li>"P" document published prior to the international filing date but later than the priority date claimed</li> </ul>	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  "&" document member of the same patent family
Date of the actual completion of the international search  11 May 2005	Date of mailing of the International search report  2 3 08 2005
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo ni,  Fax: (+31-70) 340-3016	Authorized officer  Madlener, M

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ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
Citation of document, with indication, where appropriate, of the relevant passages	TION WILL TO GLAMFITTO
& DATABASE GENESEQ 18 August 2003 (2003-08-18), retrieved from EMBL	1-12
abstract	19,20
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abstract page 3, line 30 - page 4, line 5	19,20
& DATABASE G 7 August 2003 (2003-08-07), retrieved from EMBL	1-12
Database accession no. AAE3/115 abstract	19,20
KAMATA TOMOYUKI ET AL: "R-spondin, a novel gene with thrombospondin type 1 domain, was expressed in the dorsal neural tube and affected in Whts mutants." BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1676, no. 1, 5 January 2004 (2004-01-05), pages 51-62, XP002326104 ISSN: 0006-3002 abstract page 60, right-hand column, paragraph 2 page 61	1-12,19, 20
CHEN JIN-ZHONG ET AL: "Cloning and identification of a cDNA that encodes a novel human protein with thrombospondin type I repeat domain, hPWTSR." MOLECULAR BIOLOGY REPORTS, vol. 29, no. 3, September 2002 (2002-09), pages 287-292, XP002326105 ISSN: 0301-4851 cited in the application the whole document	1-12,19, 20
BRANTJES HELEN ET AL: "TCF: Lady Justice casting the final verdict on the outcome of Wnt signalling." BIOLOGICAL CHEMISTRY. FEB 2002, vol. 383, no. 2, February 2002 (2002-02), pages 255-261, XP002326402 ISSN: 1431-6730 the whole document	19,20
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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
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Α .	ES VAN J H ET AL: "You Wnt some, you lose some: Oncogenes in the Wnt signaling pathway" CURRENT OPINION IN GENETICS & DEVELOPMENT, CURRENT BIOLOGY LTD, vol. 13, no. 1, 20 February 2003 (2003-02-20), pages 28-33, XP002249368 ISSN: 0959-437X the whole document	19,20	
A	BIENZ M ET AL: "Linking colorectal cancer to Wnt signaling" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 103, 13 October 2000 (2000-10-13), pages 311-320, XP002174510 ISSN: 0092-8674 cited in the application the whole document	19,20	
A	PEIFER M ET AL: "Wnt signaling in oncogenesis and embryogenesis-a look outside the nucleus" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 287, no. 5458, 3 March 2000 (2000-03-03), pages 1606-1609, XP002240707 ISSN: 0036-8075 cited in the application the whole document	19,20	
A	GILES R H ET AL: "Caught up in a Wnt storm: Wnt signaling in cancer" BBA - REVIEWS ON CANCER, ELSEVIER SCIENCE BV, AMSTERDAM, NL, vol. 1653, no. 1, 5 June 2003 (2003-06-05), pages 1-24, XP004427852 ISSN: 0304-419X the whole document	19,20	
	KAZANSKAYA OLGA ET AL: "R-Spondin2 is a secreted activator of Wht/beta-catenin signaling and is required for Xenopus myogenesis."  DEVELOPMENTAL CELL. OCT 2004, vol. 7, no. 4, 11 October 2004 (2004-10-11), pages 525-534, XP009046814 ISSN: 1534-5807 the whole document	1-12,19,	

lational application No. PCT/EP2004/011269

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. X Claims Nos.: 13-18 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-20-(partially)
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 13-18

Present claims 13-18 relate to an extremely large number of possible compounds/products, namely to any activator/agonist, inhibitor/antagonist or binding partner of a futrin. These compounds are defined merely by being obtainable via the methods of claims 1-12 of the present application. However, neither the claims nor the description of the present application disclose any structural features of these compounds. Thus, claims 13-18 are considered to lack clarity within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT to an extent that a meaningful search over the whole or even over a part of the claimed scope is impossible.

Consequently, no search has been carried out for claims 13-18.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20 (partially)

Diagnostic compositions involving / diagnostic uses of futrin 1 nucleic acid molecules, peptides or ligands; method of diagnosing a disease associated with aberrant expression or activity of futrin 1; method of identifying and obtaining a drug candidate for therapy of such a disease; method for identifying binding partners to / (ant)agonists of futrin 1; use of a futrin 1 activity-encoding nucleotide molecule, a futrin 1-polypeptide, an activator/agonist of a futrin 1 polypeptide or binding partner thereof for the preparation of a pharmaceutical composition for activating or inhibiting the Wnt signal cascade.

2. claims: 1-20 (partially)

Diagnostic compositions involving / diagnostic uses of futrin 2 nucleic acid molecules, peptides or ligands; method of diagnosing a disease associated with aberrant expression or activity of futrin 2; method of identifying and obtaining a drug candidate for therapy of such a disease; method for identifying binding partners to / (ant)agonists of futrin 2; use of a futrin 2 activity-encoding nucleotide molecule, a futrin 2-polypeptide, an activator/agonist of a futrin 2 polypeptide or binding partner thereof for the preparation of a pharmaceutical composition for activating or inhibiting the Wnt signal cascade.

3. claims: 1-20 (partially)

Diagnostic compositions involving / diagnostic uses of futrin 3 nucleic acid molecules, peptides or ligands; method of diagnosing a disease associated with aberrant expression or activity of futrin 3; method of identifying and obtaining a drug candidate for therapy of such a disease; method for identifying binding partners to / (ant)agonists of futrin 3; use of a futrin 3 activity-encoding nucleotide molecule, a futrin 3-polypeptide, an activator/agonist of a futrin 3 polypeptide or binding partner thereof for the preparation of a pharmaceutical composition for activating or inhibiting the Wnt signal cascade.

4. claims: 1-20 (partially)

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Diagnostic compositions involving / diagnostic uses of futrin 4 nucleic acid molecules, peptides or ligands; method of diagnosing a disease associated with aberrant expression or activity of futrin 4; method of identifying and obtaining a drug candidate for therapy of such a disease; method for identifying binding partners to / (ant)agonists of futrin 4; use of a futrin 4 activity-encoding nucleotide molecule, a futrin 4-polypeptide, an activator/agonist of a futrin 4 polypeptide or binding partner thereof for the preparation of a pharmaceutical composition for activating or inhibiting the Wnt signal cascade.

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